

Fig. 1

ATGTCCATGA	ACTGCTGAGT	GGATAAACAG	CACGGGATAT	CTCTGTCTAA	- 96
AGGAATATTA	CTACACCAGG	AAAAGGACAC	ATTCGACAAC	AGGAAAGGAG	- 46
CCTGTCACAG	AAAACCACAG	TGTCCTGTGC	ATGTGACATT	TCGCC	- 1
ATG GGA AAC AAC TGT TAC AAC GTG GTG GTC ATT GTG CTG CTG CTA	45				
Mbt Gly Asn Asn Cys Tyr Asn Val Val Val Ile Val Leu Leu Leu					
GTG GGC TGT GAG AAG GTG GGA GCC GTG CAG AAC TCC TGT GAT AAC	90				
Val Gly Cys Glu Lys Val Gly Ala Val Gl n Asn Ser Cys Asp Asn					
TGT CAG CCT GGT ACT TTC TGC AGA AAA TAC AAT CCA GTC TGC AAG	135				
Cys Gl n Pro Gly Thr Phe Cys Arg Lys Tyr Asn Pro Val Cys Lys					
● H4-1BB FI ●					
AGC TGC CCT CCA AGT ACC TTC TCC AGC ATA GGT GGA CAG CCG AAC	180				
Ser Cys Pro Pro Ser Thr Phe Ser Ser Ile Gly Gly Gl n Pro Asn					
● H4-1BB FII ●					
TGT AAC ATC TGC AGA GTG TGT GCA GGC TAT TTC AGG TTC AAG AAG	225				
Cys Asn Ile Cys Arg Val Cys Ala Gly Tyr Phe Arg Phe Lys Lys					
TTT TGC TCC TCT ACC CAC AAC GCG GAG TGT GAG TGC ATT GAA GGA	270				
Phe Cys Ser Ser Thr His Asn Ala Gl u Cys Gl u Cys Ile Gl u Gly					
TTC CAT TGC TTG GGG CCA CAG TGC ACC AGA TGT GAA AAG GAC TGC	315				
Phe His Cys Leu Gly Pro Gl n Cys Thr Arg Cys Gl u Lys Asp Cys					
AGG CCT GGC CAG GAG CTA ACG AAG CAG GGT TGC AAA ACC TGT AGC	360				
Arg Pro Gly Gl n Gl u Leu Thr Lys Gl n Gl y Cys Lys Thr Cys Ser					
● H4-1BB RI ●					
TTG GGA ACA TTT AAT GAC CAG AAC GGT ACT GGC GTC TGT CGA CCC	405				
Leu Gly Thr Phe Asn Asp Gl n Asn Gly Thr Gl y Val Cys Arg Pro					
● H4-1BB RII ●					
TGG ACG AAC TGC TCT CTA GAC GGA AGG TCT GTG CTT AAG ACC GGG	450				
Trp Thr Asn Cys Ser Leu Asp Gly Arg Ser Val Leu Lys Thr Gly					
ACC ACG GAG AAG GAC GTG GTG TGT GGA CCC CCT GTG GTG AGC TTC	495				
Thr Thr Gl u Lys Asp Val Val Cys Gly Pro Pro Val Val Ser Phe					
TCT CCC AGT ACC ACC ATT TCT GTG ACT CCA GAG GGA GGA CCA GGA	540				
Ser Pro Ser Thr Thr Ile Ser Val Thr Pro Gl u Gl y Gl y Pro Gly					
GGG CAC TCC TTG CAG GTC CTT ACC TTG TTC CTG GCG CTG ACA TCG	585				
Gly His Ser Leu Gl n Val Leu Thr Leu Phe Leu Ala Leu Thr Ser					
GCT TTG CTG CTG GCC CTG ATC TTC ATT ACT CTC CTG TTC TCT GTG	630				
Ala Leu Leu Leu Ala Leu Ile Phe Ile Thr Leu Leu Phe Ser Val					
CTC AAA TGG ATC AGG AAA AAA TTC CCC CAC ATA TTC AAG CAA CCA	675				
Leu Lys Trp Ile Arg Lys Lys Phe Pro His Ile Phe Lys Gl n Pro					
TTT AAG AAG ACC ACT GGA GCA GCT CAA GAG GAA GAT GCT TGT AGC	720				
Phe Lys Lys Thr Thr Gly Ala Ala Gl n Gl u Gl u Asp Ala Cys Ser					

Fig.1 cont'd

TGC CGA TGT CCA CAG GAA GAA GAA GGA GGA GGA GGA GGC TAT GAG 785
 Cys Arg Cys Pro Gln Glu Glu Glu Gly Gly Gly Gly Gly Tyr Glu

CTG TGA
 Leu ---

771

TGTACTATCC	TAGGAGATGT	GTGGGCCGAA	ACCGAGAAGC	ACTAGGACCC	821
CACCATCCTG	TGGAACAGCA	CAAGCAACCC	CACCACCCTG	TTCTTACACA	871
TCATCCTAGA	TGATGTGTGG	GCGCGCACCT	CATCCAAGTC	TCTTCTAACG	921
CTAACATATT	TGTCTTTACC	TTTTTTAAAT	CTTTTTTTAA	ATTTAAATTT	971
TATGTGTGTG	AGTGTTTTGC	CTGCCTGTAT	GCACACGTGT	GTGTGTGTGT	1021
GTGTGTGACA	CTCCTGATGC	CTGAGGAGGT	CAGAAGACAA	AGGGTTGGTT	1071
CCATAAGAAC	TGGAGTTATG	GATGGCTGTG	AGCCGGNNNG	ATAGGTCGGG	1121
ACGGAGACCT	GTCTTCTTAT	TTTAACGTGA	CTGTATATA	AAAAAAAAT	1171
GATATTTCCG	GAATTGTAGA	GATTGTCTTG	ACACCCTTCT	AGTTAATGAT	1221
CTAAGAGGAA	TTGTTGATAC	GTAGTATACT	GTATATGTGT	ATGTATATGT	1271
ATATGTATAT	ATAAGACTCT	TTTACTGTCA	AAGTCAACCT	AGAGTGTCTG	1321
GTTACCAGGT	CAATTTTATT	GGACATTTTA	CGTCACACAC	ACACACACAC	1371
ACACACACAC	ACGTTTATAC	TACGTACTGT	TATCGGTATT	CTACGTCATA	1421
TAATGGGATA	GGGTAAAAGG	AAACCAAAGA	GTGAGTGATA	TTATTGTGGA	1471
GGTGACAGAC	TACCCCTTCT	GGGTACGTAG	GGACAGACCT	CCTTCGGACT	1521
GTCTAAAAC	CCCCTTAGAA	GTCTCGTCAA	GTTCCCGGAC	GAAGAGGACA	1571
GAGGAGACAC	AGTCCGAAAA	GTTATTTTTT	CGGCAAAATC	TTTCCCTGTT	1621
TCGTGACACT	CCACCCCTTG	TGGACACTTG	AGTGTATCC	TTGCGCCGGA	1671
AGGTCAGGTG	GTACCCGTCT	GTAGGGGCGG	GGAGACAGAG	CCGCGGGGGA	1721
GCTACGAGAA	TCGACTCACA	GGGCGCCCCG	GGCTTCGCAA	ATGAAACTTT	1771
TTTAATCTCA	CAAGTTTCGT	CCGGGCTCGG	CGGACCTATG	GCGTCGATCC	1821
TTATTACCTT	ATCCTGGCGC	CAAGATAAAA	CAACCAAAAG	CCTTGACTCC	1871
GGTACTAATT	CTCCCTGCCG	GCCCCCGTAA	GCATAACGCG	GCGATCTCCA	1921
CTTTAAGAAC	CTGGCCGCGT	TCTGCCTGGT	CTCGCTTTTC	TAAACGGTTC	1971
TTACAAAAGT	AATTAGTTCT	TGCTTTTACG	CTCCAAGCTT	CTGCTAGTCT	2021
ATGGCAGCAT	CAAGGCTGGT	ATTTGCTACG	GCTGACCGCT	ACGCCGCCGC	2071
AATAAGGGTA	CTGGGCGGCC	CGTCGAAGGC	CCTTTGGTTT	CAGAAACCCA	2121
AGGCCCCCT	CATACCAACG	TTTCGACTTT	GATTCTTGCC	GGTACGTGGT	2171
GGTGGGTGCC	TTAGCTCTTT	CTCGATAGTT	AGAC		2205

Fig. 2a

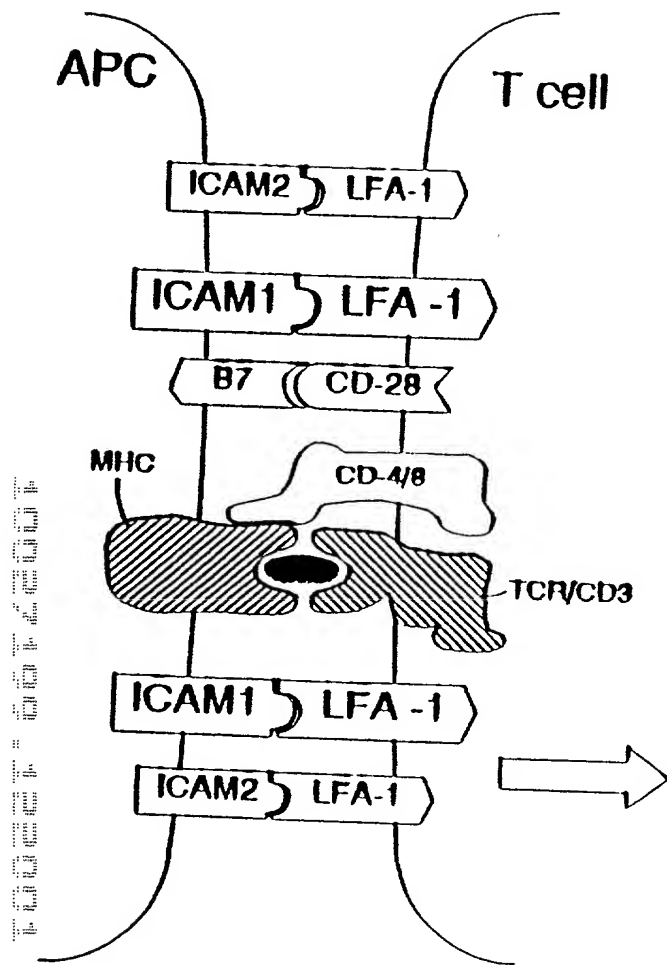
human homologue of mouse 4-1bb

h4-1bb Length 838

1 AATCAGCTTT GCTAGTATCA TACCTGTGCC AGATTTTCATC ATGGGAAACA
 51 GCTGTTACAA CATAGTAGCC ACTCTGTTGC TGGTCCTCAA CTTTGAGAGG
 101 ACAAGATCAT TGCAGGATCC TTGTAGTAAC TGCCCAGCTG GTACATTCTG
 151 TGATAATAAC AGGAATCAGA TTTGCAGTCC CTGTCCTCCA AATAGTTTCT
 201 CCAGCGCAGG TGGACAAAGG ACCTGTGACA TATGCAGGCA GTGTAAAGGT
 251 GTTTTTCAGGA CCAGGAAGGA GTGTTCTCTC ACCAGCAATG CAGAGTGTGA
 301 CTGCACTCCA GGGTTTCACT GCCTGGGGGC AGGATGCAGC ATGTGTGAAC
 351 AGGATTGTAA ACAAGGTCAA GAACTGACAA AAAAAGGTTG TAAAGACTGT
 401 TGCTTTGGGA CATTTAACGA TCAGAAACGT GGCATCTGTC GACCCTGGAC
 451 AAACTGTTCT TTGGATGGAA AGTCTGTGCT TGTGAATGGG ACGAAGGAGA
 501 GGGACGTGGT CTGTGGACCA TCTCCAGCTG ACCTCTCTCC GGGAGCATCC
 551 TCTGTGACCC CGCCTGCCCC TGCGAGAGAG CCAGGACACT CTCCGCAGAT
 601 CATCTCCTTC TTTCTTGCGC TGACGTGAC TGCCTTGCTC TTCCTGCTGT
 651 TCTTCCTCAC GCTCCGTTTC TCTGTTGTTA AACGGGGCAG AAAGAAACTC
 701 CTGTATATAT TCAAACAACC ATTTATGAGA CCAGTACAAA CTAATCAAGA
 751 GGAAGATGGC TGTAGCTGCC GATTTCCAGA AGAAGAAGAA GGAGGATGTG
 801 AACTGTGAAA TGGAAGTCAA TAGGGCTGTT GGGACTTT

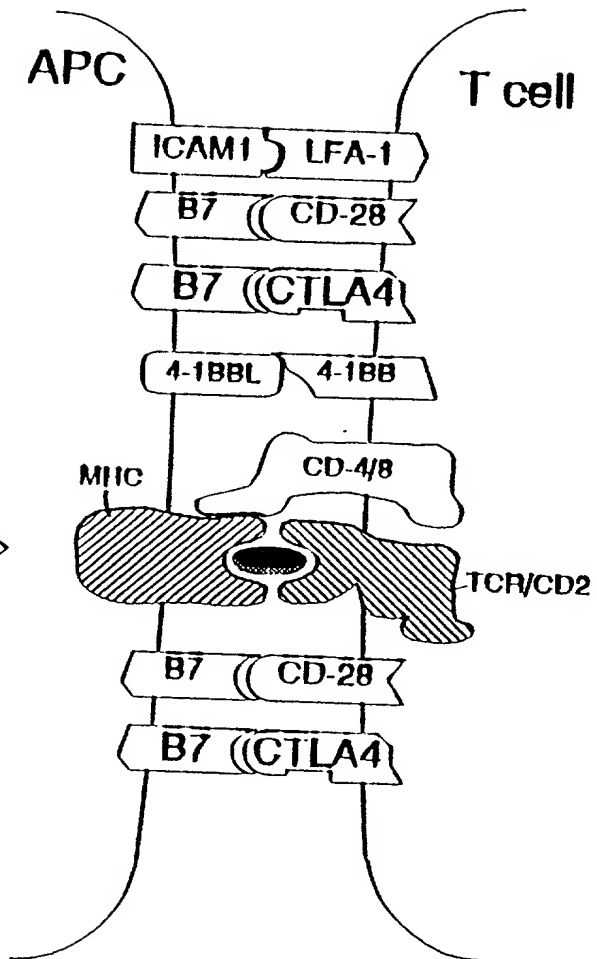
Fig. 2b

1 MGNSCYNIVA TLLLVLNFER TRSLQDFCSN CPAGTFCDNN RNQICSPCPP
 51 NSFSSAGGQR TCDICRQCKG VFRTRKECSS TSNAECDCTP GFHCLGAGCS
 101 MCEQDCKQGG ELTKKGCKDC CFGTFNDQKR GICRPWTNCS LDGKSVLVNG
 151 TKERDVVCGP SPADLSPGAS SVTPPAPARE FGHSPQIISF FLALTSTALL
 201 FLLFFLTLRF SVVKRGRKKL LYIFKQPFMR PVQTTQEEDG CSCRFPEEEE
 251 GGCEL



COGNITIVE PHASE
early activation

Fig. 3a



PROLIFERATION
CLONAL EXPANSION
late activation

Fig. 3b

NORMAL T-CELL ACTIVATION PATHWAY

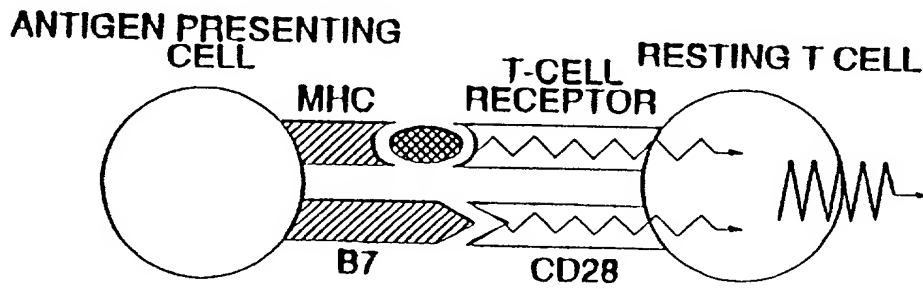


Fig. 4a

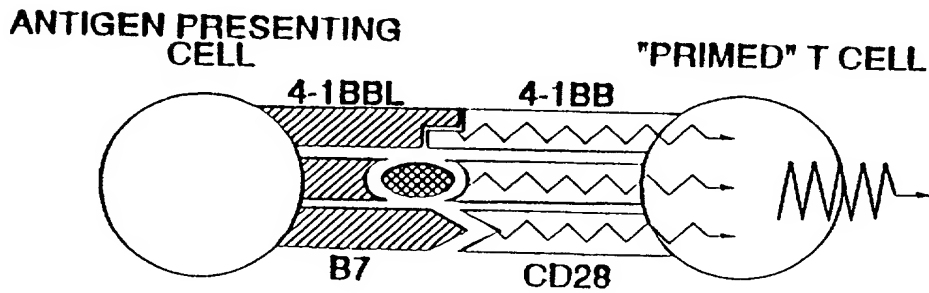


Fig. 4b

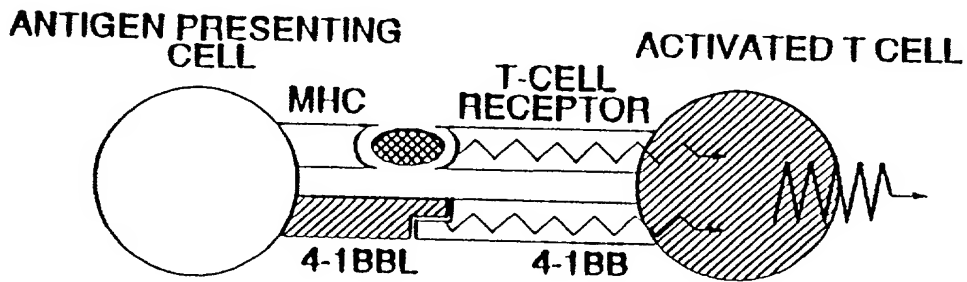
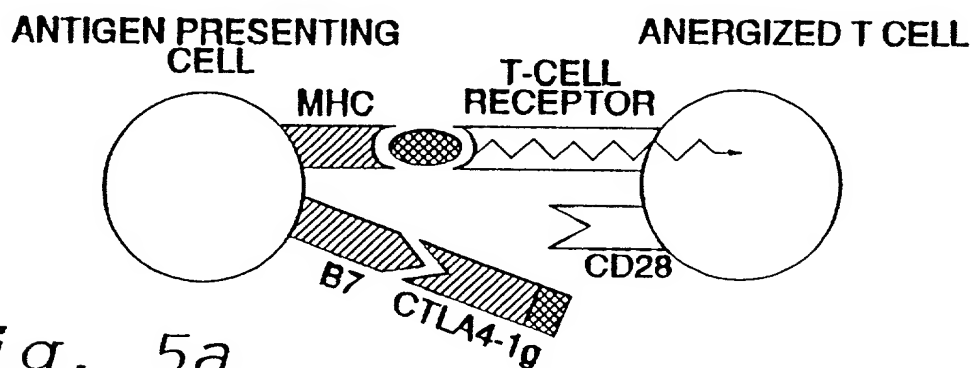
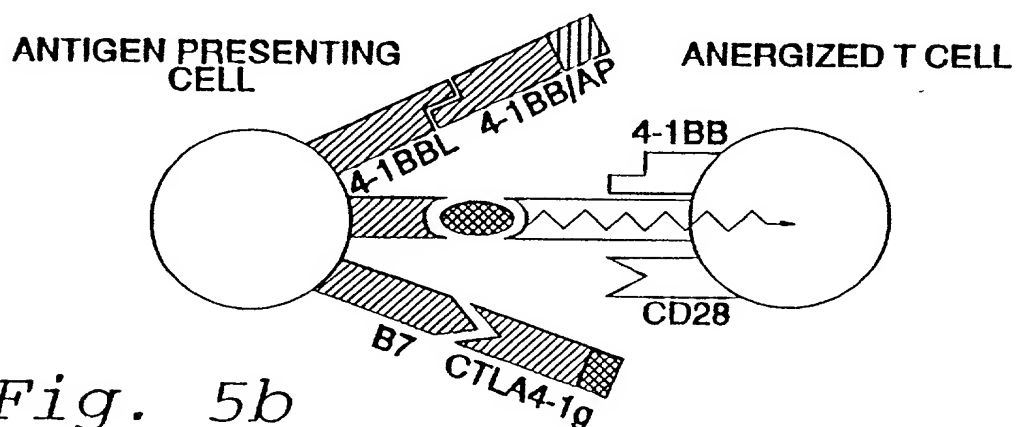
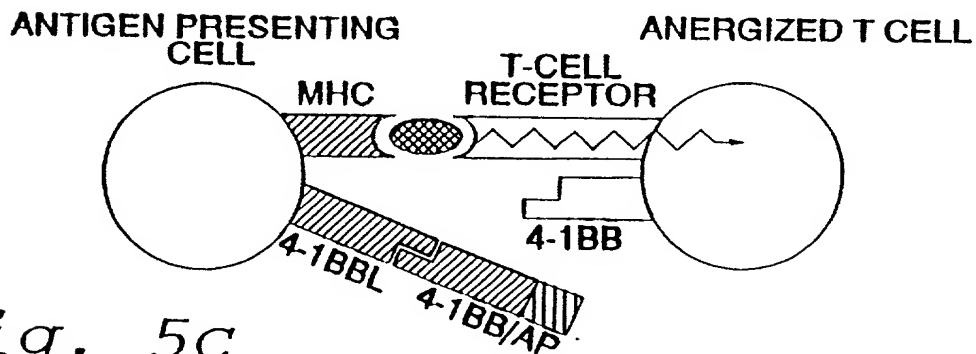


Fig. 4c

BLOCKING STEPS IN T-CELL ACTIVATION PATHWAY

*Fig. 5a**Fig. 5b**Fig. 5c*